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What is claimed is:

1. An isolated polynucleotide encoding a carboxylesterase capable of metabolizing a chemotherapeutic prodrug and inactive metabolites thereof to active drug.
- 5 2. The isolated polynucleotide of claim 1 consisting of a cDNA of Figure 4 (SEQ ID NO:20).
3. The isolated polynucleotide of claim 1 consisting of a cDNA encoding a carboxylesterase consisting of amino acids 1-543 of Figure 4 (SEQ ID NO:26).
- 10 4. An isolated polynucleotide capable of hybridizing with a polynucleotide of claim 1.
5. A vector comprising the polynucleotide of claim 1.
6. A host cell comprising the vector of claim 5.
7. A polypeptide encoded by the polynucleotide of
15 claim 1.
8. A composition comprising the polynucleotide of claim 1 and a disease-specific responsive promoter.
9. The composition of claim 8 wherein said disease-
20 specific responsive promoter is a myc promoter.
10. The composition of claim 9 wherein the myc promoter is ODC.
11. A method for sensitizing tumor cells to a chemotherapeutic prodrug comprising transfecting selected
25 tumor cells with the composition of claim 8.
12. A method of inhibiting tumor cell growth comprising:

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(a) sensitizing tumor cells in accordance with the method of claim 11; and

(b) contacting said sensitized tumor cells with a chemotherapeutic prodrug so that tumor cell growth is inhibited.

13. The method of claim 12 wherein the chemotherapeutic prodrug is selected from a group consisting of CPT-11 and APC.

14. A method of inhibiting tumor recurrence in a patient comprising:

- 10 (a) surgically removing a tumor from a patient;
(b) administering the composition of claim 8 at the site of tumor resection; and
(c) administering a chemotherapeutic prodrug systemically so that tumor recurrence is inhibited.

15 15. The method of claim 14 wherein the chemotherapeutic prodrug is selected from a group consisting of CPT-11 and APC.

16. A method of purging bone marrow cells of tumor cells comprising:

- 20 (a) removing bone marrow cells from a patient; and
(b) contacting the bone marrow cells with the composition of claim 8 and a chemotherapeutic prodrug.

17. A method of inhibiting tumor growth in a patient comprising administering to a patient a composition of claim 8 and APC.

25 18. A drug screening assay for identifying drugs that are activated by a carboxylesterase enzyme comprising:

- (a) transfecting cells in culture with the polynucleotide of claim 1;
(b) contacting said cells with a candidate drug; and
30 (c) determining growth or survival of said cells in the presence of the candidate drug.

AMENDED CLAIMS

[received by the International Bureau on 05 August 1999 (05.08.99);
new claims 20, 21 and 22 added; remaining claims unchanged (1 page)]

19. A drug screening assay for identifying compounds containing a COOC ester linkage that are activated by a carboxylesterase enzyme comprising:

(a) adding a known concentration of a test compound containing a COOC ester linkage to an assay tube containing a biological buffer and a polypeptide of claim 7;

(b) incubating the assay tubes; and

(c) analyzing contents of the assay tube for cleavage fragments of the test compound at the COOC ester linkage wherein the presence of the cleavage fragment is indicative of activation of the compound by the carboxylesterase enzyme.

20. A method for delivering carboxylesterases to selected tumor cells comprising:

(a) selecting an antibody specific for a marker on the selected tumor cells;

(b) conjugating the tumor-specific marker antibody to the carboxylesterase to form a complex; and

(c) administering the complex so that the carboxylesterases are delivered to the selected tumor cells.

21. A method of inhibiting growth of selected tumor cells in a patient comprising delivering to the selected tumor cells in the patient carboxylesterases in accordance with the method of claim 20.

22. The method of claim 21 further comprising administering to the patient a chemotherapeutic prodrug and inactive metabolites thereof which are metabolized to active drug by carboxylesterases.

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